REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and these remarks.

Cancellation is requested for claims 1-26, 29, and 30. Claims 27 and 28 are currently amended, and claims 31-44 are added. Upon entry of this response, therefore, claims 27, 28, and 31-44 will be pending.

I. Claim Rejection Under 35 USC §112, first paragraph

On pages 2 to 3 of the Office Action, Examiner Chen has rejected claims 27 and 28 on the ground that the present specification is enabling of claims directed to "inhibition" but not to "prevention" of bone mineral density reduction. In support of her position, the examiner asserts that, in "order to be enabled for prevention of a condition, applicant must demonstrate that the invention is able to prevent the condition each and every instance of that condition" (*id.* at page 3, second paragraph).

As a matter of law, however, this assertion is erroneous. The question on point is not whether applicant has shown the claimed methodology to be preventative in every instance of reduced bone mineral density. What preventative treatment or, indeed, any medical treatment is effective in every instance? Rather, the question is whether the examiner has sustained the her burden to raise a reasonable issue that "the experimentation needed to practice the invention undue or unreasonable" (MPEP § 2164.01).

For a therapeutic methodology, this question devolves to whether, pursuant to the examiner's demonstration of record, there is reasonable doubt that implementing the claimed invention for a given patient, either to prevent or to inhibit bone mineral density reduction, as the case may be, requires more than the routine endeavor of a clinician informed by the present application. In this regard, the examiner cites Pajouhi *et al.*, *Iranian J. Publ. Health* (2004), pages 57-63, for the proposition that "the art teaches bone mineral density reduction prevention is not accepted because many risk factors such as diet, age, race and family history cannot be controlled." Action at page 3, lines 12-15. To the contrary, however, Pajouhi *et al.* report on an epidemiological analysis of osteoporosis, the first such "comprehensive study ... performed in

Iran," to qualify the very factors of "race, age, sex, environment[] and nutrition" to which the examiner alludes. Rather than proposing that the incidence of such factors somehow means that "prevention is not accepted," as the examiner contends, Pajouhi *et al.* actually conclude that "[p]eak bone density in the 25-35-year-old population could be useful in policy-making ***for prevention*** and treatment of osteoporosis" (abstract; emphasis added).

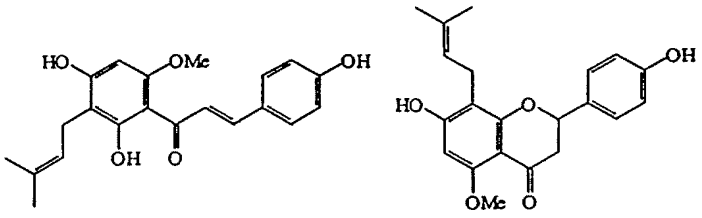
The examiner also has asserted that the present "specification does not set forth any evidence that the claimed product is able to prevent bone mineral density reduction for all potential causes" thereof. In addition the legal error in this contention, as noted above, the examiner errs in overlooking, for instance, "test 4" of applicant's working example and related commentary, e.g., at page 13, lines 10-30. These passages evidence that isoxanthohumol significantly improves the bone mineral density reduction effected by blocking ovarian estrogen secretion. Furthermore, "test 2" of the working example demonstrates, via *in vitro* data, that isoxanthohumol has estrogen activity. So informed, the skilled person would appreciate that a bone mineral density reduction caused by blocking of estrogen secretion can be prevented by intake of isoxanthohumol, in accordance with the claimed invention.

Thus, the record is devoid of any reasonable basis for questioning the presumptively enabling disclosure of the present application. See MPEP § 2164.04, citing *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) (absent such basis, a "specification disclosure which contains a teaching of the manner and process of ... using an invention in terms which correspond in scope to those used in ... defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement"). For this reason, applicant respectfully requests that Examiner Chen reconsider and withdraw the rejection discussed in this section.

II. Claim Rejections Under 35 USC §102 and §103

The examiner has rejected claims 27 and 28 for alleged anticipation by each of Erdelmeier *et al.*, WO 03/014287, and Tobe *et al.*, U.S. patent No. 5,679,716, and for alleged obviousness the combination of the Erdelmeier and Tobe references with Stevens *et al.*, *J. Chromatography A* 832: 97-107 (1999).

According to the examiner, the relevant teachings of each of the Erdelmeier and Tobe references relate to xanthohumol, a prenylchalcone which is 3'-prenyl-6'-0-methylchalconnaringenin. As shown below, xanthohumol differs in chemical structure from isoxanthohumol, a prenylflavanone:



Xanthohumol **Isoxanthohumol**

Since the rejected claims presently recite isoxanthohumol, the examiner's stated rationale for alleging anticipation is inapposite. Applicant would only add that Erdelmeier *et al.* do mention isoxanthohumol (see table on page 20) as well as osteoporosis, but only as respective members of listings of various active compounds and diseases. For this reason, too, the examiner has not made out a sustainable case for anticipation under Section 102(b)

These deficiencies in the primary references cited under Section 103(a), Erdelmeier and Tobe, are not remedied by the secondary reference, Stevens, which simply discloses the presence of isoxanthohumol in hop extract, beer, and tea. Thus, no reasonable permutation of teachings gleaned from the three cited publications could have led the skilled artisan to the use of isoxanthohumol as an active ingredient against bone mineral density reduction, as presently claimed.

It necessarily follows, therefore, that the prior art of record does not support a *prima facie* case of obviousness in this regard. Applicant also would emphasize that the use of isoxanthohumol, as claimed, gives rise to an unexpectedly beneficial effect in inhibiting or preventing bone mineral density reduction. As evidenced by "Test 4" in applicant's example (specification at page 33, line 21 to page 35, line 4), isoxanthohumol significantly ameliorated bone mineral density reduction, an effect not observed with either xanthohumol or 8-prenylnaringenin, both of which are disclosed by the Erdelmeier and Tobe references. This surprising superiority of isoxanthohumol, vis-à-vis bone mineral density reduction, belies the contention of obviousness advanced by the examiner. In addition, this result is achieved without

undesirable side effects through estrogen action, such as an increased risk for metrorrhagia, breast cancer, and uterine cancer. See specification at page 5, lines 25 to 34, and page 34, line 34 to page 35, line 4. By contrast, 8-prenylnaringenin has a strong estrogen activity, as applicant's Figure 2 shows in its comparison of the impact on uterine weight of isoxanthohumol (IXH) versus 8-prenylnaringenin (8PN) at 5 and 25 mg/kg.

At least for these reasons, the examiner is asked to reconsider and withdraw not only the anticipation rejection but also the obviousness rejection of claims 27 and 28.

CONCLUSION

Applicant submits that the present application is in condition for allowance. An early indication to this effect is requested, therefore. Examiner Chen also is invited to contact the undersigned directly, should she feel than any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If an extension is needed for timely acceptance of submitted papers, then applicant hereby petitions for such extension under 37 CFR §1.136 and authorizes payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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